



ADNP syndrome

ADNP syndrome is a condition that causes a wide variety of signs and symptoms. Its hallmark features are intellectual disability and autism spectrum disorder, which is characterized by impaired communication and social interaction. Affected individuals also have distinctive facial features and abnormalities of multiple body systems.

Individuals with *ADNP* syndrome have mild to severe intellectual disability and delayed development of speech and motor skills such as sitting and walking. Some affected individuals are never able to speak. People with this disorder exhibit features typical of autism spectrum disorder, including repetitive behaviors and difficulty with social interactions. *ADNP* syndrome is also associated with mood disorders or behavioral problems, such as anxiety, temper tantrums, attention deficit-hyperactivity disorder (ADHD), obsessive-compulsive disorder, or sleep problems.

Many people with *ADNP* syndrome have distinctive facial features, which most commonly include a prominent forehead, a high hairline, outside corners of the eyes that point upward or downward (upslanting or downslanting palpebral fissures), droopy eyelids (ptosis), a broad nasal bridge, and a thin upper lip. These individuals may also have unusually shaped ears or hand and finger abnormalities. Eye and vision abnormalities, such as eyes that do not point in the same direction (strabismus) and farsightedness (hyperopia), also occur in *ADNP* syndrome. Some people with this condition have early appearance (eruption) of primary (baby) teeth.

Some people with *ADNP* syndrome have weak muscle tone (hypotonia) and feeding difficulties in infancy. They may also have digestive system problems, such as backflow of stomach acids into the esophagus (gastroesophageal reflux), vomiting, and constipation. Other features that occur in *ADNP* syndrome include obesity, seizures, and heart abnormalities.

Frequency

The prevalence of *ADNP* syndrome is unknown. It is estimated to account for 0.17 percent of all cases of autism spectrum disorder, making it one of the most common genetic causes of this condition.

Genetic Changes

ADNP syndrome is caused by mutations in the *ADNP* gene. The protein produced from this gene helps control the activity (expression) of other genes through a process called chromatin remodeling. Chromatin is the network of DNA and protein that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression

is regulated during development; when DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

By regulating gene expression, the ADNP protein is involved in many aspects of growth and development. It is particularly important for regulation of genes involved in normal brain development, and it likely controls the activity of genes that direct the development and function of other body systems.

Although it is unclear how mutations in the *ADNP* gene affect ADNP protein function, researchers suggest that the mutations result in abnormal chromatin remodeling. Disturbance of this process alters the activity of many genes and disrupts development or function of several of the body's tissues and organs, including the brain. These changes likely explain the intellectual disability, autism spectrum disorder, and other diverse signs and symptoms of *ADNP* syndrome.

Inheritance Pattern

ADNP syndrome is not inherited. It results from new (de novo) mutations in the *ADNP* gene that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. The condition occurs in people with no history of the disorder in their family.

Other Names for This Condition

- ADNP-related intellectual disability and autism spectrum disorder
- ADNP-related multiple congenital anomalies-intellectual disability-autism spectrum disorder
- Helsmoortel-van der Aa syndrome
- HVDAS
- mental retardation, autosomal dominant 28
- MRD28

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Helsmoortel-van der aa syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/CN189714/>

Other Diagnosis and Management Resources

- GeneReview: ADNP-Related Intellectual Disability and Autism Spectrum Disorder
<https://www.ncbi.nlm.nih.gov/books/NBK355518>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Autism Spectrum Disorder
<https://medlineplus.gov/ency/article/001526.htm>
- Encyclopedia: Intellectual Disability
<https://medlineplus.gov/ency/article/001523.htm>
- Health Topic: Autism Spectrum Disorder
<https://medlineplus.gov/autismspectrumdisorder.html>
- Health Topic: Developmental Disabilities
<https://medlineplus.gov/developmentaldisabilities.html>

Genetic and Rare Diseases Information Center

- ADNP syndrome
<https://rarediseases.info.nih.gov/diseases/12931/adnp-syndrome>

Additional NIH Resources

- National Institute of Neurologic Disorders and Stroke: Autism Spectrum Disorder Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Autism-Spectrum-Disorder-Information-Page>

Educational Resources

- Centers For Disease Control and Prevention: Facts About Intellectual Disability
https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/intellectualdisability.pdf
- MalaCards: adnp syndrome
http://www.malacards.org/card/adnp_syndrome

- Merck Manual Consumer Version: Intellectual Disability
<http://www.merckmanuals.com/home/children-s-health-issues/learning-and-developmental-disorders/intellectual-disability>
- Orphanet: ADNP-related multiple congenital anomalies-intellectual disability-autism spectrum disorder
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=404448

Patient Support and Advocacy Resources

- ADNP Kids Research Foundation
<http://www.adnpkids-researchfoundation.org/>
- American Association on Intellectual and Developmental Disabilities
<http://aaidd.org/>
- Autism Society
<http://www.autism-society.org/>
- Autism Speaks
<https://www.autismspeaks.org/>
- Simons VIP Connect: ADNP gene
<https://www.simonsvipconnect.org/what-we-study/single-genes.html?id=544>
- The Arc: For People with Intellectual and Developmental Disabilities
<http://www.thearc.org/>

GeneReviews

- ADNP-Related Intellectual Disability and Autism Spectrum Disorder
<https://www.ncbi.nlm.nih.gov/books/NBK355518>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ADNP+syndrome%5BTIAB%5D%29+OR+%28Helsmoortel-van+der+Aa+syndrome%5BTIAB%5D%29%29+OR+%28%28ADNP%5BTIAB%5D%29+AND+%28autism%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- HELSMOORTELE-VAN DER AA SYNDROME
<http://omim.org/entry/615873>

MedGen

- MENTAL RETARDATION, AUTOSOMAL DOMINANT 28
<http://www.ncbi.nlm.nih.gov/medgen/862975>

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<https://ghr.nlm.nih.gov/condition/adnp-syndrome>

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